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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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*Ex parte* JAY A. GOLDSTEIN, MICHAEL ROTHMAN,
and WHE-YONG LO

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Appeal 2010-006562
Application 10/691,928
Technology Center 1600

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Before TONI R. SCHEINER, LORA M. GREEN, and STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a topical antifungal composition and a method of treating a fungal disease. The Patent Examiner rejected the claims on the grounds of anticipation and obviousness. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part.

## STATEMENT OF THE CASE

The invention relates to topical formulations containing an antifungal agent and an anti-inflammatory steroid. (Spec. 1.) According to the Specification, "[s]teroids can penetrate the skin and cause undesirable side effects" (*id.*), but "[a] low potency steroid agent minimizes side effects such as skin atrophy, striae and hypopigmentation" (*id.* at 2.)

Claims 1-17, which are all the pending claims, are on appeal. Claim 1 is representative and reads as follows:

1. A topical antifungal composition comprising:
a) a therapeutically effective amount of an antifungal compound for treating a fungal disease or a pharmaceutically acceptable salt thereof; and
b) a therapeutically effective amount of a low to low-medium potency steroidal anti-inflammatory causing minimal skin atrophy, striae and hypopigmentation, in a concentration between 0.01 wt% and 5.0 wt%, and having a higher potency than 1 wt% hydrocortisone, and
c) a carrier suitable for administration of the antifungal compound and the steroidal anti-inflammatory to the skin, wherein the composition does not cause the steroids to penetrate the skin and cause undesirable local side effects.

The Examiner rejected the claims as follows:

- claims 1 and 8-13 under 35 U.S.C. § 102(b) as anticipated by Quigley;[1]
- claims 1-3, 8-13, and 17 under 35 U.S.C. § 102(b) as anticipated by Burnett;[2]
- claims 1-3 and 7-17 under 35 U.S.C. § 103(a) as unpatentable over Quigley; and

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[1] John W. Quigley, Jr., et al., US 6,075,056, issued June 13, 2000.
[2] Katherine M. Burnett et al., US 6,238,683 B1, issued May 29, 2001.

• claims 1-13 and 17 under 35 U.S.C. § 103(a) as unpatentable over Burnett and Shah.[3]

ANTICIPATION

*The Rejection over Quigley*

The rejection cited many of Quigley's teachings describing steroid and antifungal compositions (Ans. 3-4), and ultimately found that "one of ordinary skill in the art would immediately envisage a composition comprising all the ingredients listed in Table G [of Quigley], except substituting terbinafine or naftifine for butenafine" (*id.* at 4). As the envisaged composition, substituting terbinafine or naftifine where Quigley used butenafine, would be one of Appellants' compositions, the rejection found the claims anticipated.

Appellants contend that (1) Quigley "does not disclose selecting the claimed class of steroidal anti-inflammatory in combination with an antifungal as required by the claims" (App. Br. 11); (2) "neither [Quigley's] prophetic formulations nor the exemplified compositions constitute an anticipation of claim 1" (*id.*); (3) "to arrive at formulations within the scope of claim 1 from the myriad of [Quigley's formulations] would require significant picking and choosing" (*id.* at 12); and (4) Quigley's examples containing 0.064 wt% betamethasone dipropionate appear to be more potent than the claimed compositions (*id.*).

We agree with Appellants that Quigley did not describe the claimed composition in the manner required to find anticipation under § 102(b), because Quigley provided multiple, distinct teachings of compositions, but

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[3] Hemanshu S. Shah et al., US 5,219,877, issued June 15, 1993.

not of a composition of steroid and antifungal as defined in Appellants' claims. *See Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008) ("unless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102. . . . it is not enough that the prior art reference . . . includes multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention").

*The Rejection over Burnett*

Burnett described a topical composition comprising the antifungal ketoconazole, the steroid desonide, and a penetration enhancer, among other ingredients. (Ans. 4.) Nortwithstanding the fact that Burnett used a penetration enhancer, and Appellants' claimed "composition does not cause the steroids to penetrate the skin and cause undesirable local side effects" (Claim 1, part c), the rejection directed attention to Burnett's disclosure that its "composition of Example 1 demonstrated positively less permeation through the skin into the receptor that could clinically translate into lower systemic toxicity." (Burnett, col. 8, ll. 45-59, cited at Ans. 5.) The Examiner found that Burnett's composition was "disclosed not to penetrate through the skin," disclosure consistent with Appellants' claim 1, part c, non-penetration requirement. (Ans. 5.)

Appellants contend that Burnett requires a penetration enhancer, "but the use of a penetration enhancer causes the steroidal anti-inflammatory to penetrate into the dermis, leading to higher potency of the anti-inflammatory and risking the side effects Appellants avoid. Further, the use of a

penetration enhancer also causes the anti-fungal portion of the composition to be less efficacious at the epidermis, which is the site of the fungal infection." (*Id.* at 14.) Appellants contrast their invention as using "a carrier . . . which does not cause the steroids to penetrate the skin and cause undesirable side effects." (*Id.* at 14.)

The evidence is that Burnett described a composition whose steroids did penetrate the skin. According to Burnett, limited penetration caused fewer *systemic* side effects, but the rejection does not provide evidence that Burnett's composition met the particular claimed requirement that the composition not cause undesirable *local* side effects. Anticipation requires that a prior art reference disclose every limitation of the claimed invention, either explicitly or inherently. *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997). Because the rejection presents insufficient evidence that Burnett's composition had every property defined in claim 1, it must be reversed.

OBVIOUSNESS

*The Rejection over Quigley*

The rejection relied in part on the Examiner's earlier findings concerning Quigley's disclosure. (Ans. 6, citing the findings set out at Ans. 3-4.) Additional findings were that Quigley taught a lotion comprising an antifungal, a low-mid strength steroidal anti-inflammatory 0.01 to 0.1% betamethasone dipropionate, and excipients that "don't afford steroidal penetration of the epidermis," as well as a cream comprising 0.05% desonide. (Ans. 6.) The Examiner pointed out that desonide is the steroid required in some of Appellants' claims. (*Id.*) Claim 5 in fact recites "0.01 wt % to 5.0 wt % desonide."

Appellants dispute that Quigley "disclose[d] or suggest[ed] compositions containing a therapeutically effective amount of an antifungal compound for treating a fungal disease . . . and a therapeutically effective amount of a low to low-medium potency steroidal anti-inflammatory causing minimal skin atrophy, striae and hypopigmentation as required by the claims." (App. Br. 17.) As an initial matter, this generalized argument is unpersuasive because it fails to account for the undisputed fact that Quigley taught using 0.05% desonide and Appellants' compositions explicitly include 0.05% desonide. More particularly, the Examiner directed attention to Quigley's disclosure that a disadvantage of steroids is that "[s]teroids can penetrate the skin and cause undesirable side effects, including skin atrophy . . . ." (Quigley at col. 1, ll. 26-30, cited by the Examiner at Ans. 3.) Further, the Examiner directed attention to Quigley's preference for the steroid betamethasone dipropionate at concentrations within the range recited in Appellants' claims. (Ans. 6.) The fact that Quigley recognized that steroids may penetrate the skin and cause side effects such as skin atrophy means that a person of ordinary skill in the art would have been aware of that potential complication, and would have taken it into account when following Quigley's formulation teachings. Accordingly, we agree with the Examiner that "it would have been *prima facie* obvious for one of ordinary skill in the art to formulate topical compositions according to Quigley et al. comprising low to low-medium potency steroids." (Ans. 12.)

Appellants contend that the Goldstein Declaration[4] "presented data which clearly shows the criticality of the small set of steroidal anti-inflammatories specified in the claims and shows unexpected results across this small set." (App. Br. 17-18.) The Appeal Brief explains:

> The data in Dr. Goldstein's declaration not only demonstrates the unexpected efficacy and lack of side effects of one non-halogenated steroidal anti-inflammatory, desonide, in combination with an antifungal but additional data is presented showing the same unexpected efficacy and lack of side effects for other members of the claimed class of low to low-mid potency steroidal antiinflammatories. Members of the claimed class that have been shown to produce results comparable to a topical cream containing 0.05% desonide and 1 % clotrimazole are: . . . .

(App. Br. 18.)

> Declarant states:
>
> I began using anti-fungal preparations in conjunction with low potency topical steroids on my patients with inflammatory tinea, and found that in fact such preparations were both safe and effective. They shortened the time to clearing of the fungus, and they dramatically decreased the symptoms of redness and especially itching.

(Decl. 2, ¶ 3.)

The Declaration provides five case reports and summarizes as follows:

> In summary, oxicanozole cream 1% with hydrocortisone cream 2½% applied twice daily and econazole cream 1 % with fluocinalone acetonide cream 0.01 % applied twice daily resulted in marked clearing of pruritus and the eruption at 3 weeks. Clotrimazole 1% cream with acalmetasone dipropionate 0.05% cream applied twice

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[4] Declaration Under 37 C.F.R. § 1.132, by Jay A. Goldstein, signed Feb. 26, 2007.

> daily was effective in completely clearing long standing recurrent tinea cruris, after several weeks of usage. Econazole cream 1% with alclometasone dipropionate 0.05% applied twice daily resulted in marked clearing of eruption in a patient with a history of tinea.

(Decl. 5, ¶ 10.)

"[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) ("Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention"). "[B]y definition, any superior property must be *unexpected* to be considered evidence of non-obviousness. Thus, in order to properly evaluate whether a superior property was unexpected, the [fact-finder] should . . . consider[ ] what properties were expected." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1371 (Fed. Cir. 2007).

Although Appellants state that the results shown in the Declaration were unexpected, they have not shown that results would have been unexpected by a person of ordinary skill in the art. As the Examiner noted, Quigley described the problem of steroid induced side effects such as skin atrophy in antifungal compositions with steroids. Quigley followed the identification of the side-effect problem by touting a corresponding advantage of its own composition: "it delivers the antifungal agent and the steroid to the skin, but minimizes the penetration of the skin with respect to the steroid, thus avoiding the potential side effects attendant upon prolonged steroid use." (Quigley at col. 2, ll. 23-27.)

The Declaration's results therefore do not appear to have been unexpected because Quigley taught compositions of the same steroids, listed

in its low to medium potency group, and combined with antifungals, as topical antifungal compositions: hydrocortisone cream (albeit at a lower concentration), fluocinalone acetonide cream 0.01%, and aclometasone dipropionate cream 0.05%. (Quigley at col. 5.) The Declaration thus confirms Quigley's teachings for those steroids, but does not show, for example, that other steroids Quigley taught as low to medium potency would not have produced the same or similar results. Without a fair comparative showing that there is an unexpected result compared to the dozens of low to medium potency steroids Quigley taught, it appears that the Declaration only confirms what would have true of all Quigley's low to medium strength steroids, as Quigley indicated. We note the Declaration's concern with using formulations of stronger, more potent steroids (Decl. 2-3, ¶ 3), but as Quigley taught multiple low to medium potency steroids in its groups we see no reasonable basis to excuse the lack of a comparative showing against at least that closest prior art.

After reassessing all the evidence, we conclude that the weight of the evidence favors the conclusion of obviousness. Claims 2, 3, and 7-17 have not been argued separately and therefore stand or fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

*The Rejection over Burnett and Shah*

The rejection is based on a finding, among others, that Burnett described a composition that "does not permeate through the skin." (Ans. 8.) The rejection also relied on Shah as evidence supporting the obviousness of using clotrimazole as the antifungal in a Burnett-type composition and method. (*Id.* at 9.)

Appellants dispute that Burnett "disclose[d] or suggest[ed] compositions containing a therapeutically effective amount of a low to low-medium potency steroidal anti-inflammatory causing minimal skin atrophy, striae and hypopigmentation, in a concentration between 0.01 wt% and 5.0 wt%, and having a higher potency than 1 wt% hydrocortisone, and wherein the composition does not cause the steroids to penetrate the skin and cause undesirable local side effects as required by claim 1." (*Id.* at 20.)

We disagree with the Examiner that Burnett described a composition "wherein the composition does not cause the steroids to penetrate the skin and cause undesirable local side effects," as required by claim 1, part c. See the discussion of the Burnett reference in the Anticipation section above. The rejection does not account for that difference between Burnett's composition and the composition defined in Appellants' claim 1. Because every claim limitation is not accounted for, the rejection is reversed. *See In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (when concluding that a claim would have been obvious, the rejection must evidence "a searching comparison of the claimed invention – including all its limitations – with the teachings of the prior art").

## SUMMARY

We reverse the rejection of claims 1 and 8-13 under 35 U.S.C. § 102(b) as anticipated by Quigley.

We reverse the rejection of claims 1-3, 8-13, and 17 under 35 U.S.C. § 102(b) as anticipated by Burnett.

We affirm the rejection of claims 1-3 and 7-17 under 35 U.S.C. § 103(a) as unpatentable over Quigley.

We reverse the rejection of claims 1-13 and 17 under 35 U.S.C. § 103(a) as unpatentable over Burnett and Shah.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

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